

BuSpar® (buspirone HCl)

References: 1. Newton RE, et al. A review of the side effect profile of buspirone. *Am J Med* 1986;80(3B):17-21. 2. Moskowitz H and Smiley A. Effects of chronically administered buspirone and diazepam on driving-related skills performance. *Clin Psychopharmacol* 1982;43(12 Suppl 2):45-55. 3. Lader M. Assessing the potential for buspirone dependence or abuse and effects of its withdrawal. *Am J Med* 1987;82(SA):20-26.

Contraindications: Hypersensitivity to buspirone.

Warnings: The administration of BuSpar to a patient taking a monoamine oxidase inhibitor (MAOI) may pose a hazard. Since blood pressure has become elevated when BuSpar was administered concomitantly with an MAOI, such concomitant use is not recommended. BuSpar should not be employed in lieu of appropriate antipsychotic treatment.

Precautions: General—Interference with cognitive and motor performance: Although buspirone is less sedating than other anxiolytics and does not produce significant functional impairment, its CNS effects in a given patient may not be predictable; therefore, patients should be cautioned about operating an automobile or using complex machinery until they are reasonably certain that buspirone does not affect them adversely. Although buspirone has not been shown to increase alcohol-induced impairment in motor and mental performance, it is prudent to avoid concomitant use with alcohol.

Potential for withdrawal reactions in sedative/hypnotic/anticholinergic drug dependent patients: Because buspirone will not block the withdrawal syndrome often seen with cessation of therapy with benzodiazepines and other common sedative/hypnotic drugs, before starting buspirone withdraw patients gradually from their prior treatment, especially those who used a CNS depressant chronically. Rebound or withdrawal symptoms may occur over varying time periods, depending in part on the type of drug and its elimination half-life. The withdrawal syndrome can appear as any combination of irritability, anxiety, agitation, insomnia, tremor, abdominal cramps, muscle cramps, vomiting, sweating, flu-like symptoms without fever, and occasionally, even as seizures.

Possible concerns related to buspirone's binding to dopamine receptors: Because buspirone can bind to central dopamine receptors, a question has been raised about its potential to cause acute and chronic changes in dopamine mediated neurological function (e.g., dystonia, pseudoparkinsonism, akathisia, and tardive dyskinesia). Clinical experience in controlled trials has failed to identify any significant neuroleptic-like activity; however, a syndrome of restlessness, appearing shortly after initiation of treatment, has been reported; the syndrome may be due to increased central noradrenergic activity or may be attributable to dopaminergic effects (ie, represent akathisia).

Information for Patients—Patients should be instructed to inform their physician about any medications, prescription or non-prescription, alcohol or drugs they are now taking or plan to take during treatment with buspirone; to inform their physician if they are pregnant, are planning to become pregnant, or become pregnant while taking buspirone; to inform their physician if they are breast feeding; and not to drive a car or operate potentially dangerous machinery until they experience how this medication affects them.

Drug Interactions—Concomitant use with other CNS active drugs should be approached with caution (see **Warnings**). Concomitant use with trazodone may have caused 3- to 6-fold elevations on SGPT (ALT) in a few patients. Buspirone does not displace lightly bound drugs like phenytoin, propranolol, and warfarin from serum proteins, but may displace less firmly bound drugs like digoxin.

Carcinogenesis, Mutagenesis, Impairment of Fertility—No evidence of carcinogenic potential was observed in rats or mice; buspirone did not induce point mutations, nor was DNA damage observed; chromosomal aberrations or abnormalities did not occur.

Pregnancy: Teratogenic Effects—Pregnancy Category B: Should be used during pregnancy only if clearly needed.

Nursing Mothers—Administration to nursing women should be avoided if clinically possible.

Pediatric Use—The safety and effectiveness have not been determined in individuals below 18 years of age. **Use in the Elderly—**No unusual, adverse, age-related phenomena have been identified in elderly patients receiving a total, modal daily dose of 15 mg.

Use in Patients with Impaired Hepatic or Renal Function—Since buspirone is metabolized by the liver and excreted by the kidneys, it is not recommended in severe hepatic or renal impairment.

Adverse Reactions (See also Precautions): Commonly Observed—The more commonly observed untoward events include dizziness, nausea, headache, nervousness, lightheadedness, and excitement.

Associated with Discontinuation of Treatment—The more common events causing discontinuation included: central nervous system disturbances (3.4%), primarily dizziness, insomnia, nervousness, drowsiness, lightheaded feeling; gastrointestinal disturbances (1.2%), primarily nausea; miscellaneous disturbances (1.1%), primarily headache and fatigue. In addition, 3.4% of patients had multiple complaints, none of which could be characterized as primary.

Incidence in Controlled Clinical Trials—Adverse events reported by 1% or more of 477 patients who received buspirone in four-week, controlled trials: **Cardiovascular:** Tachycardia/palpitations 1%, CNS: Dizziness 12%, drowsiness 10%, nervousness 5%, insomnia 3%, lightheadedness 3%, decreased concentration 2%, excitement 2%, anger/hostility 2%, confusion 2%, depression 2%, **EENT:** Blurred vision 2%, **Gastrointestinal:** Nausea 8%, dry mouth 3%, abdominal/gastric distress 2%, diarrhea 2%, constipation 1%, vomiting 1%, **Musculoskeletal:** Musculoskeletal aches/pains 1%, **Neurological:** Numbness 2%, paresthesia 1%, incoordination 1%, tremor 1%, **Skin:** Skin rash 1%, **Miscellaneous:** Headache 6%, fatigue 4%, weakness 2%, sweating/clamminess 1%.

Other Events Observed During the Entire Pre-marketing Evaluation—The relative frequency of all other undesirable events reasonably associated with the use of buspirone in approximately 3000 subjects who took multiple doses of the drug under well-controlled, open, and uncontrolled conditions is defined as follows: Frequent are those occurring in at least 1/100 patients; infrequent are those occurring in 1/100 to 1/1000 patients; and rare are those occurring in less than 1/1000 patients. **Cardiovascular—**frequent: non-specific chest pain; infrequent: syncope, hypotension, hypertension; rare: cerebrovascular accident, congestive heart failure, myocardial infarction, cardiomyopathy, bradycardia. **Central Nervous System—**frequent: dream disturbances; infrequent: depersonalization, dysphoria, noise intolerance, euphoria, akathisia, fearfulness, loss of interest, disassociative reaction, hallucinations, suicidal ideation, seizures; rare: feelings of claustrophobia, cold intolerance, stupor, slurred speech, psychosis. **EENT—**frequent: tinnitus, sore throat, nasal congestion; infrequent: redness and itching of the eyes, altered taste, altered smell, conjunctivitis; rare: inner ear abnormality, eye pain, photophobia, pressure on eyes. **Endocrine—**rare: galactorrhea, thyroid abnormality. **Gastrointestinal—**infrequent: flatulence, anorexia, increased appetite, salivation, irritable colon, rectal bleeding; rare: burning of the tongue. **Genitourinary—**infrequent: urinary frequency, urinary hesitancy, menstrual irregularity and spotting, dysuria; rare: amenorrhea, pelvic inflammatory disease, enuresis, nocturia. **Musculoskeletal—**infrequent: muscle cramps, muscle spasms, rigid/stiff muscles, arthralgias. **Neurological—**infrequent: involuntary movements, slowed reaction time; rare: muscle weakness. **Respiratory—**infrequent: hyperventilation, shortness of breath, chest congestion; rare: epistaxis. **Sexual Function—**infrequent: decreased or increased libido; rare: delayed ejaculation, impotence. **Skin—**infrequent: edema, pruritus, flushing, easy bruising, hair loss, dry skin, facial edema, blisters; rare: acne, thinning of nails. **Clinical Laboratory—**infrequent: increases in hepatic aminotransferases (SGOT, SGPT); rare: eosinophilia, leukopenia, thrombocytopenia. **Miscellaneous—**infrequent: weight gain, fever, roaring sensation in the head, weight loss, malaise; rare: alcohol abuse, bleeding disturbance, loss of voice, hiccoughs.

Drug Abuse and Dependence: Controlled Substance Class—Not a controlled substance.

Physical and Psychological Dependence—Buspirone has shown no potential for abuse or diversion and there is no evidence that it causes tolerance, or either physical or psychological dependence. However, since it is difficult to predict from experiments the extent to which a CNS active drug will be misused, diverted, and/or abused once marketed, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of buspirone misuse or abuse (e.g., development of tolerance, incrementation of dose, drug-seeking behavior).

Overdosage: Signs and Symptoms—At doses approaching 375 mg/day the following symptoms were observed: nausea, vomiting, dizziness, drowsiness, miosis, and gastric distress. No deaths have been reported in humans either with deliberate or accidental overdosage.

Recommended Overdose Treatment—General symptomatic and supportive measures should be used along with immediate gastric lavage. No specific antidote is known and dialyzability of buspirone has not been determined.

For complete details, see Prescribing Information or consult your Mead Johnson Pharmaceuticals Representative.

U.S. Patent Nos. 3,717,634 and 4,182,763

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Books Received

Books received by THE WESTERN JOURNAL OF MEDICINE are acknowledged in this column. Selections will be made for more extensive review in the interest of readers as space permits.

MOLECULAR GENETICS IN MEDICINE—Vol 7 in Progress in Medical Genetics—Edited by Barton Childs, MD, Professor Emeritus; Neil A. Holtzman, MD, Professor; Haig H. Kazazian, Jr, MD, Professor; and David L. Valle, MD, Professor, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore. Elsevier, 52 Vanderbilt Ave, New York, NY 10017, 1987. 245 pages, \$45.

MONITORING AND EVALUATION—ANESTHESIA SERVICES. Joint Commission on Accreditation of Healthcare Organizations, 875 N Michigan Ave, Chicago, IL 60611, 1987. 56 pages, \$30 (paperback).

MONITORING AND EVALUATION—PHYSICAL REHABILITATION SERVICES. Joint Commission on Accreditation of Healthcare Organizations, 875 N Michigan Ave, Chicago, IL 60611, 1988. 68 pages, \$30 (paperback).

MONITORING AND EVALUATION OF THE QUALITY AND APPROPRIATENESS OF CARE—A HOME CARE EXAMPLE. Joint Commission on Accreditation of Healthcare Organizations, 875 N Michigan Ave, Chicago, IL 60611, 1988. 21 pages, \$5 (paperback).

OCCUPATIONAL BACK PAIN—Vol. 2, No. 1 of SPINE: STATE OF THE ART REVIEWS—Edited by Richard A. Deyo, MD, MPH, Director, Health Services Research and Development, Seattle Veterans Administration Medical Center, and Associate Professor, Department of Medicine and of Health Services, University of Washington School of Medicine, Seattle. Hanley & Belfus, Inc, 210 S 13th St, Philadelphia, PA 19107, 1987. 165 pages; \$32 (single issue), \$75 (subscription, 3 issues per year).

OCULOPLASTIC, ORBITAL, AND RECONSTRUCTIVE SURGERY—Volume One—EYELIDS—Edited by Albert Hornblass, MD, Clinical Professor of Ophthalmology, State University of New York, Health Science Center at Brooklyn, and Director of Ophthalmic Plastic, Orbital and Reconstructive Surgery, Manhattan Eye, Ear and Throat Hospital; Lenox Hill Hospital; and State University of New York Health Science Center at Brooklyn. Williams & Wilkins, 428 E Preston St, Baltimore, MD 21202, 1988. 703 pages, \$125.

QUALITY AND HOME HEALTH CARE—REDEFINING THE TRADITION. Joint Commission on Accreditation of Healthcare Organizations, 1987. 127 pages, \$30 (paperback).

THE SHOULDER—Edited by Carter R. Rowe, MD, Associate Clinical Professor (Emeritus), Department of Orthopaedic Surgery, Harvard Medical School, and Senior Surgeon, Department of Orthopaedics, Massachusetts General Hospital, Boston. Churchill Livingstone Inc, 1560 Broadway, New York, NY 10036, 1987. 654 pages, \$140.

SICKLE CELL ANEMIA AND THALASSEMIA—A PRIMER FOR HEALTH CARE PROFESSIONALS—R. G. Huntsman, MD (Cantab), FRCP (UK), Medical Director, Canadian Sickle Cell Society and Canadian Red Cross Blood Transfusion Service, and Professor of Pathology (Hematology), Memorial University of Newfoundland. Canadian Sickle Cell Society, PO Box 13156, Station A, St John's, Newfoundland, Canada A1B 4A4, 1987. 204 pages, \$10 (paperback).

TEMPORARY CARDIAC PACING—Carl E. Bartecchi, MD, Clinical Professor, Departments of Medicine and Family Medicine, University of Colorado School of Medicine. Precept Press, 160 E Illinois St, Chicago, IL 60611, 1987. 212 pages, \$45 (clothbound).

THE TRAGEDY OF BLACK LUNG—FEDERAL COMPENSATION FOR OCCUPATIONAL DISEASE—Peter S. Barth, Professor of Economics, University of Connecticut, and formerly Executive Director, National Commission on State Workmen's Compensation Laws. W. E. Upjohn Institute for Employment Research, 300 S Westnedge Ave, Kalamazoo, MI 49007, 1987. 285 pages, \$11.95 (paperback), \$16.95 (cloth).

UROLOGY—Problems in Primary Care Series—Edited by Elroy D. Kursh, MD, Associate Professor of Surgery/Urology, and Martin I. Resnick, MD, Professor and Chairman, Division of Urology, Case Western Reserve University School of Medicine, Cleveland. Medical Economics Books, Oradell, NJ 07649, 1987. 322 pages, \$32.95 (softbound).

WRONG DIAGNOSIS—WRONG TREATMENT—THE PLIGHT OF THE ALCOHOLIC IN AMERICA—Joseph D. Beasley, MD, Medical Director, Brunswick House, Amityville, Long Island, New York. Creative Informatics, Inc, PO Box 1607, Durant, OK 74702-1607, 1987. 268 pages, \$12.95 (paperback).

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